THE PREVENTION AND TREATMENT OF CONVULSIVE DISORDERS*

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THE subject for our discussion tonight has for a score of centuries been the picnic-ground for a merry-go-round of inconclusive thinking. The twenty-seven different names which have been applied to convulsions and their contradictory connotations are evidence for this statement.

The "Sacred Disease" is opposed by the "Demon Disease"; the "Shining Disease" by the "Black Disease"; "St. Anthony Disease" by the "Filthy Disease." However, non-committal descriptive terms have survived longest, "Commitialis Morbus," "The Falling Sickness," "Epilepsy" and our English, "Fits."

"Paroxysmal Convulsive Disorders," the choice of the American Neurological Association and hence, out of courtesy, my title for this evening, represents an effort to escape the fear and loathing which has encrusted the term "epilepsy" in its passage through the Dark Ages. The effort is commendable but the choice defeats its own purpose. "Convulsive Disorders" centers attention on the convulsion, the most fearful aspect of a seizure. "Disorders of Consciousness" would be a preferable term for two reasons. First, loss or impairment of consciousness is less feared than a convulsion; syncope is commonplace; sleep is an every day, or every night, occurrence. Second, and more important, loss of consciousness is the central sun of the constellation of symptoms which make up a seizure. The seizure most distinctive of epilepsy, both clinically and electrically, is the petit mal, a transient loss of consciousness accompanied by the three-per-second alternate dart-and-dome dysrhythmia. This form of seizure is relatively more common in so-called "essential epilepsy," is not reproducible by artificial means, such as the use of convulsant drugs, and constitutes abou 70 per cent of all seizures. Both consideration for patients and scientific accuracy vote for the

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term "disorders of consciousness." Objection that there are many forms of unconsciousness can be countered by mention of the many conditions in which involuntary convulsive muscular movements are the presenting symptom—chorea, tetany, habit spasms, eclampsia, hiccup, sneezing, orgasm, and so forth.

Tempering the wind to the shorn lamb is an act of mercy and the physician in speaking to his patient often finds use for wishful words which also conceal: spasmophilia, pyknolepsy, fainting spells, or nervous turns. If we wish to go the whole way in both camouflage and scientific accuracy, the proper expression is "symptomatic cerebral dysrhythmia."[1] However, sugar-coating is neither desirable nor necessary in this medical presence and with your permission, I shall substitute the unpleasantly familiar term "epilepsy" for the multiform "convulsive disorders."

Traditionally, etiological factors have been separated into two distinct groups. First is the so-called "idiopathic" or "cryptogenic epilepsy," seizures out of the nowhere into the here. The word "idiopathic" means "one's own suffering"—a condition, the cause of which is not extrinsic but arises out of one's own peculiar make-up, an inborn characteristic. The terms "idiopathic," "constitutional," and "hereditary" would seem to be interchangeable. In the second group, symptomatic epilepsy, seizures are the result of some pathology of body or brain. The last five years have altered 500-year-old conceptions. Idiopathic epilepsy is no longer a Jovian thunderbolt out of the blue, unpredictable and inscrutable, but is a disturbance in the chemical makeup or reactions of the discharging cells of the brain. This chemical disorder results in a disturbance in the orderly pulsations of the electrical currents of the brain and these electrical pulsations as recorded seem to be a hereditary trait. Studies of the brain-wave records of the epileptic and his relatives bring support to the suggestion that an underlying defect has been transmitted. Epilepsy is a double-headed dragon, but with only one heart, cerebral dysrhythmia, a heart which a daring Saint George M.D. will someday pierce. Instead of the obscure ancient terms "idiopathic" and "symptomatic," I propose the clear-cut terms "genetic" and "acquired."

This terminology has the advantage of placing epilepsy on the same footing as other metabolic diseases. The word "idiopathic" or "cryptogenic" implies an origin which is mysterious, and unknowable, a sort of

spontaneous combustion of devastating symptoms. "Genetic" implies predisposition or more specifically genes and chromosomes and their chemical structures which, if they cannot be seen, can at least be visualized. "Acquired" is entirely distinct from "genetic" and yet the processes are complementary. Modern geneticists emphasize what clinicians have postulated for centuries, namely, that heredity and environment are complementary factors whose joint action produce many of the ills which beset body and brain. Diabetes, hypertension, tuberculosis, obesity, cancer are but examples of scores of disease conditions which are both transmitted and acquired. Seed and soil combine to make a plant; spark and gunpowder, to make an explosion. Although in the great majority of patients both factors are at work, their relative importance varies from patient to patient. Probably the case is rare in which only heredity or only an acquired cause is responsible for seizures. Nevertheless, these two categories are clinically useful, if, when we speak of either genetic or acquired epilepsy, we recognize the probability that acquired or genetic factors respectively are also partially responsible. I stress this point because a comprehensive and effective program of treatment must be based on a recognition of multiple causes in the individual patient.

Prevention: If, as a general rule, "an ounce of prevention is worth a pound of cure," then in epilepsy a milligram of prevention would be worth a kilogram of cure. During the last twenty years I have examined thousands of articles which dealt with the subject of epilepsy but remember only a few which attacked the important subject of prevention. This neglect is due to the fact that a seizure is almost always a complete surprise to all concerned. "We never dreamed," say the parents, "that such a thing could happen to our child." Eighty-three per cent will add, "There has never been a case like this on either side." The doctor examines the patient, pronounces him sound and healthy, and mutters to himself. "Cryptogenic"—born of secrecy—"epilepsy." Having no conception of a cause, he cannot conceive prevention, though he may be able to provide symptomatic treatment.

As I have stated, there are two general causes of seizures, genetic and acquired, and in any given patient the twin influences are at work. However, in three fourths of patients, the genetic forces seem to prevail, and in one-fourth, one or more of the environmental factors. In spite of this preponderance, geneticists warn that even if sterilization of

epileptics were universally applied, benefit to future generations would be negligible, because the vastly more numerous "carriers" transmit the disorder as readily as epileptics but cannot be identified. We are able to stress prevention by means of eugenics only because of the almost telepathic aid given by the electroencephalogram.

This is not the occasion for a presentation of laboratory data but I need to say that Dr. and Mrs. Gibbs and I have made and classified electroencephalograms of 1,000 normal control persons, 1,260 epileptics, 320 near relatives of epileptics, and 80 twins (160 co-twins), identical and non-identical, epileptic and non-epileptic.[2,3,4] Study of these data leads to these conclusions: the pattern of brain waves is an hereditary trait; epilepsy, per se, is not inherited, but a predisposition is, and in most persons this predisposition, if present, is represented as an abnormality in the electroenchephalogram. The brain-wave pattern is not fixed but a fluid trait and various considerations blunt the sharpness of the deductions which can be drawn from it. Nevertheless, this technique seems to make it possible to trace the underground asymptomatic course of epilepsy through the generations, to give advice about marriage and childbearing based on individual rather than on general facts and possibly to take the offensive against epilepsy by starting treatment before the seizures begin.

Thus, the prevention of epilepsy by means of eugenics, requires the dying out or the breeding out of hereditary dysrhythmia. The question of whether transmitted dysrhythmia is a dominant or a recessive, and whether disordered brain waves could be "bred out" by crossing with ordered brain waves, must await the collection of more data and the decision of geneticists. Moreover, given a person whose electroencephalogram is abnormal, we must know that his dysrhythmia is transmitted and not acquired, and we must learn the genetic significance of various degrees and types of abnormality. It would now seem that epilepsy will be the chief beneficiary of this study, for of all neuropsychiatric disorders, dysrhythmia seems to be most consistently present (85 to 90 per cent) in persons subject to seizures. In epileptics the most distinctive abnormality is the intermittent appearance on the electroencephalographic record of short bursts of high-voltage waves which may be abnormally fast, slow, or else alternately fast or slow—what the Gibbs call "seizure-discharges." Records with this type of disturbance are found 33 times more frequently in epileptics and 7.7 times

more frequently in their relatives than in a control population. The corresponding multiples for records without seizure-discharges, but which are grossly slow or fast, are 19 times and 4.8 times. The multiples for records which are only moderately slow or fast are 2.3 and 2.9 times. Pushing the comparison still farther, in epileptics paroxysmal discharges are 13 times more important than moderate slowness or fastness of rate, and in the relatives of epileptics, they are three times more important. The proportion of petit mal patients in the group is influential in studies of this sort, for 86 per cent of patients who have only petit mal have records classed as paroxysmal against 45 per cent of patients who have only psychomotor seizures, and 17 per cent of patients who have only grand mal.[2]

Hereditary dysrhythmia can be prevented only by means of eugenics, either by forbidding progeny to all persons with transmitted and serious brain-wave disorders—an imposing task—or perhaps by dilution of the trait through their marriage with persons possessed of normal brain waves. On the other hand, even if a disordered pattern of brain waves has been inherited, epilepsy itself may possibly be prevented if environmental conditions which act as precipitants of seizures can be avoided. I refer to trauma received at birth or later in life from traffic or industrial accidents or from wounds received in war, certain infections which invade the brain or meninges, encephalitis, meningitis, whooping-cough, and syphilis, certain severe circulatory or emotional disturbances, and many convulsant drugs, the most common of which is alcohol. Prevention of these precipitating conditions lies partly with the public and its elected representatives and partly with the individual.

Finally, whether an observed dysrhythmia is transmitted or acquired there is the possibility of preventing the appearance of clinical manifestations through the use of anticonvulsant drugs in the pre-seizure period. This possibility has not as yet been tested. Obviously, it would be more apropos in children, in persons with definite seizure-discharges, and in those who have a previous history of brain injury or have displayed symptoms which might be premonitory—an infantile convulsion, temper tantrums, enuresis, periods of unexplained sleep, dizziness, falling, head-nodding, and so forth. Without the aid of the electroencephalogram, preventive measures must deal with such relatively indirect matters as better obstetrics, fewer wars, and a clearer recognition of premonitory symptoms.

Treatment: Insofar as treatment is based on etiology, the search for the cause or causes of seizures must be highly individualized. This requires careful history-taking and painstaking examinations. One must attempt to rule out each of the dozens of conditions which, if present, act as contributing causes for convulsions. Most prominent of these conditions are congenital maldevelopments, birth or later brain trauma, brain or meningeal infections, intracranial tumors, circulatory lesions, severe metabolic or endocrine abnormalities, toxemias, convulsant drugs, and borderline states simulating epilepsy. These latter embrace syncope, irritable carotid sinus, vasovagal seizures, hysteria, and eclampsia. A shrewd guess as to the presence or absence of one of these conditions can be made on the basis of a careful history and physical and neurological examination; in other words, at an office visit. However, the unexpected happens often enough to justify certain laboratory examinations as a routine. These include Roentgen-rays of the skull, urine and blood examinations, morphological and chemical, and in early cases, or in patients with localized symptoms, spinal fluid examination and possibly a pneumoencephalogram. In our experience, most important of the methods of examination is the recording of the electrical activity of the brain of the patient, and of his parents or other near relatives. These records give some idea of the relative importance of genetic and acquired causes, and of the type, severity, and localization of the disorder.

Corrective treatment is based on the elimination of abnormalities which seem to have a direct responsibility for seizures. The chief of these are tumors or scars of the brain which can be removed by the neurosurgeon, a task requiring the best of skill and judgment.

However, the activity of the brain is indirectly influenced by each body organ and cell and modern physicians do well to repeat some of the rules of health prescribed by Hippocrates. The maintenance of a healthy body and a confident mind, and participation in the work of the world is good medicine for all patients.

If, as happens in at least 95 per cent of patients, neurosurgery has nothing to offer, the physician has to rely chiefly on drug therapy. We preach the necessity of rational therapy, yet for these thousands of years the control of seizures has been empirical. Bromides and phenobarbital apparently act by virtue of their sedative action. They are general soothers of nervous activity and not correctives of the specific disorder of epilepsy. Dilantin sodium, on the other hand, seems to be of specific

value in certain types of epilepsy. Whether it improves the abnormal chemistry of neuronal cells which causes their disorderly and excessive discharge is a subject for future research.

Dilantin sodium was not stumbled on by accident but was the result of planned and patient search. I am sure I express the feelings of tens of thousands when I praise the Chairman of the Fortnight Committee, Dr. Tracy J. Putnam. He, it was who refused to believe that the chance discoveries of Locock and Hauptman could not be improved on by conscientious search. He, with Dr. H. H. Merritt, initiated the studies which led to the demonstration of the superior effectiveness of this non-sedative drug over the previously used sedatives. Dilantin sodium is the drug of choice for most patients subject to seizures. Epilepsy is a tough disease. Dilantin is a sharp weapon which must be wielded skillfully. In the beginning the physician must see the patient at frequent intervals in order to steer him safely between the rocks of toxicity and the whirlpool of continued seizures. The guiding principle is to increase the dose of Dilantin by gradual steps until a maximum therapeutic result is achieved or until symptoms of toxicity appear. The use of Dilantin sodium (phenytoin sodium), as explained in detail by Merritt and Putnam[5] and others[6] need not be repeated here. The matter of dosage requires reiteration. Many physicians who think of phenobarbital and phenytoin sodium in the same quantitative terms, have patients who say, "Dilantin does not seem to work with me." For most patients, the dosage of Dilantin should at least double that of phenobarbital, from 4½ to 9 grains (0.3 to 0.6 gm.) a day.

Pleased as we are with finding this better weapon in our hands, the electroencephalograph warns against undue optimism. Improvement of brain waves usually lags far behind reduction in the number of seizures. Petit mal (dart-and-dome dysrhythmias) are often made worse by Dilantin. The problem of epilepsy will not be solved until cortical dysrhythmia can be controlled.

In addition to drugs, the physician should make use of social and psychological therapy. In my experience, the lot of almost every patient can be improved by attention to these domains. Not only can the physician help his patient by encouragement in intellectual and vocational pursuits, by reorientation of the attitude and hopes of the patient and his family, but he can also do much to correct the present deplorable attitude of the general public. A sign of the times is the formation

of the Laymen's League Against Epilepsy, a national organization with the twin aims of public education and encouragement of research.[7] Local groups are also being organized. Large potentialities for good lie in the New York Society of Convulsive Disorders.

Problems of War and Epilepsy: Our thinking at present revolves around the means for survival in a world convulsed with war. Immediate medical problems are two. First is the duty of keeping epileptics out of the armed forces. The wisdom of this rigid policy may be questioned on the grounds that specially chosen patients when geared to special jobs might be outstandingly useful. In addition, there is the long-standing warning of geneticists that subjecting only the most fit to death and destruction is slow national suicide. Second is the problem of assimilating epileptics into industries which are suddenly labor-hungry. For the person subject to seizures, these two problems are cumulative. A history of seizures automatically throws the draftee into the bottom drawer of the discarded, a drawer marked *4-F*. This procedure, in turn, automatically spoils his chances for work. "If the Army doctors say his physical condition is hopeless," reasons the employer, "I don't want him."

A further barrier to employment which operates in peace, as well as in war times, is the fear of the employer that he may be held responsible for any injury which the epileptic might sustain as a result of a fit "on the job." We have circularized the various states in the Union, asking about compensation codes as they affect the epileptic who may be injured while at work.[8] Replies received from thirty-eight states indicate a lack of any uniformity in the laws or their interpretation. Of court decisions made in five of the states, two ruled that the company was liable even though a seizure caused the fall and the death. "A workman carries with him all his disabilities." At first glance, decisions which provide compensation to the epileptic whatever the circumstances would seem favorable to him. Practically, such decisions are disadvantageous. Because of them, or because of uncertainty in regard to liability, most employers will not knowingly hire an epileptic. It would seem only just that the epileptic should be permitted to waive his rights to compensation when injury results from a spontaneous seizure while at work. In only seven states does there seem to be a provision that an employee may reject the Compensation Act.

Even broader barriers to securing employment are the fear and horror which the sight of a convulsion produces in fellow employees,

the conception of an epileptic as a deteriorated, cantankerous or physically ineffective person who would not be worth his wages, and ignorance of the fact that new methods of diagnosis and treatment are now available. To gather information on the employment record of epileptics we have analyzed the histories of about 1,000 adult clinic and private patients, many of these furnished by colleagues throughout the country. Except for the temporary effects of disuse, the bodily machine of the epileptic is as sound as the average of the population. Not more than 10 or 15 per cent had disturbances of muscular power, coördination, or of control which would prove a serious handicap in physical work. Two-thirds of these patients were judged to be mentally normal by the examining neurologist. Of 608 men who answered the question about their ability to work, 54 per cent were fully able, 24 per cent were partially able, and 22 per cent were unable to work, for the most part because of seizures. Of the 407 women the corresponding percentages were 48 per cent, 34 per cent, and 18 per cent. Of 571 men who answered the question about employment, 97 per cent had formerly been employed, but only 73 per cent had a position when seen by the examining neurologist. Of the 410 males who were employed at the time of examination, 11 per cent were in a profession, 30 per cent in business, 22 per cent in skilled and 37 per cent in unskilled labor. The various occupations were distributed widely over the field of possible occupations.[8]

The adult epileptics in the United States when projected on the number of persons "gainfully employed" form an army of approximately 350,000 persons. A considerable proportion of this force, perhaps a quarter or a third, are unfit for productive activity. Too many of the remaining quarter million persons are denied a share in the work of the world because of public neglect, ignorance and prejudice. Physicians who prescribe inactivity for their patients, who do not know and practice recently acquired facts, who do not join in the campaign against epilepsy, must share the blame.

After the war is over both the relative and the absolute numbers of epileptics will be greatly increased. None will be killed in service but judging from the last war, from 5 to 15 per cent of the brain-wounded will become epileptic. The proportion may be greater now because chemotherapy will save the lives of men with serious brain wounds who before would have died. The hope of decreasing the burden of trau-

matic epilepsy lies with neurosurgery and with the finding of yet more effective anticonvulsant drugs.

Conclusions

In the light of new knowledge gained through use of the electroencephalograph, the term "genetic" is suggested as a substitute for "essential," "idiopathic," or "cryptogenic" epilepsy, and the term "acquired" for "symptomatic" epilepsy. Efforts to prevent epilepsy are more feasible now than formerly. The principal agencies are: (1) the prevention of cerebral dysrhythmia, rather than of epilepsy itself, by means of eugenics; (2) the prevention of acquired conditions which act as a precipitant of seizures, and (3) possibly the treatment of persons who have either hereditary or acquired dysrhythmia in the pre-seizure period.

The important aspects of treatment are removal of acquired causes, the improvement of general physique, the use of anticonvulsant drugs, especially phenytoin sodium, and efforts to strengthen the psychological and social underpinnings of the patient.

War increases both the relative and absolute numbers of epileptics and makes it harder for those rejected by the draft to secure employment. In spite of the needs of industry, now labor-hungry, and in spite of the quarter million epileptics who are physically and mentally able to work, many thousands of persons are refused employment because of popular misinformation and prejudice, and because of compensation laws which may make the employer responsible for injury suffered as a result of a seizure. The efforts of clinicians, investigators and coöperating laymen should be intensified in and after this war period.

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